

AMENDMENTS TO THE CLAIMS:

Please amend the claims as follows:

1. (Currently Amended) A biologically active complex comprising alpha-lactalbumin and a cofactor which stabilises the complex in a biologically active form, wherein the alpha-lactalbumin is selected from the group consisting of:

- (i) an alpha-lactalbumin identified by SEQ ID NO: 1 or SEQ ID NO: 2,
- (ii) an alpha-lactalbumin variant which has at least 95 % identity to human alpha-lactalbumin as defined by SEQ ID NO: 1 or at least 95 % identity to bovine alpha-lactalbumin as defined by SEQ ID NO: 2,

wherein the cofactor is an unsaturated [[C16-C18]]C₁₆ to C₁₈ fatty acid with at least one double bond in the cis configuration with the proviso that the cofactor is not C18:1:9 cis (oleic acid).

2. (Currently Amended) A biologically active complex comprising alpha-lactalbumin and a cofactor which stabilises the complex in a biologically active form, wherein the alpha-lactalbumin is selected from the group consisting of:

- (i) an alpha-lactalbumin identified by SEQ ID NO: 1 or SEQ ID NO: 2,
- (ii) an alpha-lactalbumin variant which has at least 95 % identity to human alpha-lactalbumin as defined by SEQ ID NO: 1 or at least 95 % identity to bovine alpha-lactalbumin as defined by SEQ ID NO: 2,

wherein the cofactor is an unsaturated C₁₆ to C₁₈ fatty acid with 1 to 3 double bonds in the cis configuration with the proviso that the cofactor is not C18:1:9 cis (oleic acid)~~A complex according to claim 1 wherein the cofactor is an unsaturated C16-C18~~

~~fatty acid with 1 to 3 double bonds in the cis configuration with the proviso that the cofactor is not C18:19 cis (oleic acid).~~

3. (Previously Presented) A complex according to claim 1 wherein the cofactor is cis C18:1:11 fatty acid.

4. (Previously Presented) A complex according to claim 1 which comprises an alpha-lactalbumin variant which has at least 95 % identity to human alpha-lactalbumin as defined by SEQ ID NO: 1 or at least 95 % identity to bovine alpha-lactalbumin as defined by SEQ ID NO: 2.

5. (Currently Amended) A biologically active complex according to claim 1 which is obtainable by combining

(i) a cis unsaturated [[C16-C18]]C₁₆ to C₁₈ fatty acid with at least one double bond in the cis configuration; and

(ii)

(a) an alpha lactalbumin from which calcium ions have been removed, or

(b) a variant of alpha-lactalbumin from which calcium ions have been removed or which does not have a functional calcium binding site.

6. (Previously Presented) A complex according to claim 1 which includes an alpha-lactalbumin variant in which the calcium binding site has been modified so that the affinity for calcium is reduced, or it is no longer functional.

7. (Previously Presented) A complex according to claim 6 wherein the variant has a mutation at a position corresponding to at least one of the K79, D82, D84, D87 or D88 residues of bovine alpha-lactalbumin (SEQ ID NO:2).

8. (Previously Presented) A complex according to claim 7 which includes a D87A variant of alpha-lactalbumin (SEQ ID NO:3) or D87N variant of alpha-lactalbumin (SEQ ID NO:4).

Claim 9. (Canceled)

Claim 10. (Canceled)

11. (Previously Presented) A complex according to claim 1 wherein the alpha lactalbumin is human alpha-lactalbumin (SEQ ID NO:1).

12. (Previously Presented) A complex according to claim 1 wherein the alpha lactalbumin variant is mutant bovine alpha-lactalbumin which includes an S70R mutation (SEQ ID NO:5).

13. (Previously Presented) A complex according to claim 1 which further comprises calcium ions.

14. (Previously Presented) A pharmaceutical composition comprising a complex according to claim 1 in combination with a pharmaceutically acceptable carrier.

Claim 15. (Canceled)

Claim 16. (Canceled)

Claim 17. (Canceled)

Claim 18. (Canceled)

19. (Previously Presented) A complex according to claim 1 wherein the complex induces apoptosis selectively in tumor cells.

20. (Currently Amended) A complex according to claim 1, wherein the alpha-lactalbumin is a variant of alpha-lactalbumin containing and wherein the amino acid substitutions are conservative amino acid substitutions.

21. (Previously Presented) A complex according to claim 1, wherein the alpha-lactalbumin is a variant of alpha-lactalbumin at least 95 % identical to human alpha-lactalbumin (SEQ ID NO:1).

Claim 22. (Canceled)

23. (Previously Presented) A complex according to claim 3, wherein the alpha-lactalbumin is a variant of alpha-lactalbumin and wherein the amino acid substitutions are conservative amino acid substitutions.

24. (Previously Presented) A complex according to claim 3, wherein the variant of alpha-lactalbumin has at least 95 % identity to human alpha-lactalbumin (SEQ ID NO: 1).

Claim 25. (Canceled)

Claim 26. (Canceled)

27. (Previously Presented) The complex according to claim 1, wherein the cofactor is an unsaturated fatty acid selected from the group of: C18:1:11cis , C18:1:6cis, C18:2:9,12cis, C16:1:9cis, C18:3:6,9,12cis and C18:3:9,12,15cis.

28. (Previously Presented) The complex according to claim 1 wherein the cofactor is selected from the group of: C18:1:11cis , C18:1:6cis, C18:3:6,9,12cis and C18:3:9,12,15cis.

29. (Previously Presented) A biologically active complex comprising alpha-lactalbumin and a cofactor which stabilises the complex in a biologically active form, wherein the cofactor is oleic acid (C18:1:9_{cis}) and wherein the alpha-lactalbumin is selected from the group consisting of:

- (i) bovine alpha-lactalbumin identified by SEQ ID NO: 2, and
- (ii) an alpha-lactalbumin variant which has at least 95 % identity to human alpha-lactalbumin as defined by SEQ ID NO: 1 or at least 95 % identity to bovine alpha-lactalbumin as defined by SEQ ID NO: 2,

wherein the alpha-lactalbumin variant is not human alpha-lactalbumin as defined by SEQ ID NO: 1.

30. (Previously Presented) The complex according to claim 29 which includes an alpha-lactalbumin variant in which the calcium binding site has been modified so that the affinity for calcium is reduced, or it is no longer functional.

31. (Previously Presented) The complex according to claim 29 wherein the variant has a mutation at a position corresponding to at least one of the K79, D82, D84, D87 or D88 residues of bovine alpha-lactalbumin as defined by SEQ ID NO: 2.

32. (Previously Presented) The complex according to claim 29, which includes a D87A or D87N variant of alpha-lactalbumin as defined by SEQ ID NO: 3 and SEQ ID NO: 4, respectively.

33. (Previously Presented) The complex according to claim 29, wherein the alpha-lactalbumin variant is mutant bovine α -lactalbumin which includes an S70R mutation as defined by SEQ ID NO: 5.

34. (Previously Presented) The complex according to claim 29, wherein the alpha-lactalbumin is

- (i) bovine alpha-lactalbumin as defined by SEQ ID NO: 2 or
- (ii) an alpha-lactalbumin variant at least 95 % identical to SEQ ID NO: 1 or

SEQ ID NO: 2.

Claim 35. (Canceled)

36. (Previously Presented) A complex according to claim 29, wherein the complex induces apoptosis selectively in tumor cells.

37. (new) A complex according to claim 2 wherein the cofactor is cis C18:1:11 fatty acid.

38. (new) A complex according to claim 2 which comprises
an alpha-lactalbumin variant which has at least 95 % identity to human alpha-lactalbumin as defined by SEQ ID NO: 1 or at least 95 % identity to bovine alpha-lactalbumin as defined by SEQ ID NO: 2.

39. (new) A biologically active complex according to claim 2 which is obtainable by combining

(i) a cis unsaturated C₁₆ to C₁₈ fatty acid with 1-3 double bond in the cis configuration; and

(ii)

(a) an alpha lactalbumin from which calcium ions have been removed, or

(b) a variant of alpha-lactalbumin from which calcium ions have been removed or which does not have a functional calcium binding site.

40. (new) A complex according to claim 2 which includes an alpha-lactalbumin variant in which the calcium binding site has been modified so that the affinity for calcium is reduced, or it is no longer functional.

41. (new) A complex according to claim 40 wherein the variant has a mutation at a position corresponding to at least one of the K79, D82, D84, D87 or D88 residues of bovine alpha-lactalbumin (SEQ ID NO:2).

42. (new) A complex according to claim 41 which includes a D87A variant of alpha-lactalbumin (SEQ ID NO:3) or D87N variant of alpha-lactalbumin (SEQ ID NO:4).

43. (new) A complex according to claim 2 wherein the alpha lactalbumin is human alpha-lactalbumin (SEQ ID NO:1).

44. (new) A complex according to claim 2 wherein the alpha lactalbumin variant is mutant bovine alpha-lactalbumin which includes an S70R mutation (SEQ ID NO:5).

45. (new) A complex according to claim 2 which further comprises calcium ions.

46. (new) A pharmaceutical composition comprising a complex according to claim 2 in combination with a pharmaceutically acceptable carrier.

47. (new) A complex according to claim 2 wherein the complex induces apoptosis selectively in tumor cells.

48. (new) A complex according to claim 2, wherein the alpha-lactalbumin is a variant of alpha-lactalbumin containing conservative amino acid substitutions.

49. (new) A complex according to claim 2, wherein the alpha-lactalbumin is a variant of alpha-lactalbumin at least 95 % identical to human alpha-lactalbumin (SEQ ID NO:1).

50. (new) A complex according to claim 37, wherein the alpha-lactalbumin is a variant of alpha-lactalbumin containing conservative amino acid substitutions.

51. (new) A complex according to claim 37, wherein the variant of alpha-lactalbumin has at least 95 % identity to human alpha-lactalbumin (SEQ ID NO: 1).

52. (new) The complex according to claim 2, wherein the cofactor is an unsaturated fatty acid selected from the group of: C18:1:11cis, C18:1:6cis, C18:2:9,12cis, C16:1:9cis, C18:3:6,9,12cis and C18:3:9,12,15cis.

53. (new) The complex according to claim 2 wherein the cofactor is selected from the group of: C18:1:11cis, C18:1:6cis, C18:3:6,9,12cis and C18:3:9,12,15cis.